

~~glycation of histone H1 by ADP-ribose, (ii) admixing (i a) a substance to be tested, wherein said substance is not aminoguanidine, (ii b) histone H1, and (iii c) ADP-ribose, and determining if said substance to be tested has an effect on glycation of histone H1 by ADP-ribose, wherein indication of an effect on said glycation by comparing the levels of glycation in the two assays, wherein a change in effect on glycation as compared to the first assay indicates that said substance regulates glycation~~

- (i) admixing ADP-ribose and histone H1 and determining fluorescence,
- (ii) admixing ADP-ribose, histone H1, and said substance, and determining fluorescence,
- (iii) comparing measured fluorescence in (i) and (ii), wherein a decrease in measured fluorescence in (ii) as compared to (i) is indicative of a possible protein glycation inhibitor,
- (iv) combining said possible protein glycation inhibitor with AGE-BSA, and measuring fluorescence,
- (v) measuring fluorescence of an amount of AGE-BSA equal to that in (iv),
- (vi) comparing fluorescence in (iv) and (v), wherein a decrease of fluorescence in (iv) as compared to (v) is indicative of a false positive, which quenches AGE fluorescence, and
- (viii) combining said substance if it does not quench AGE fluorescence with a protein, and determining damage done to said protein by said substance, wherein a lack of said damage indicates said substance is an inhibitor of protein glycation.

Claim 2 (original): The method of claim 1, wherein said substance is a dicarbonyl scavenger.

Claim 3 (original): The method of claim 1, wherein said substance is not an antioxidant.

Claim 4 (canceled)

Claim 5 (canceled)

Claim 6 (currently amended): The method of claim 2 1, comprising measuring fluorescence in steps (i) and (ii) about 5 days after admixing (a), (b), and (c).

Claim 7 (canceled)

Claim 8 (currently amended): The method of claim 1, further comprising determining damage done to said protein by said substance by determining cross-linking of molecules of histone H1.

Claim 9 (original): The method of claim 1, wherein said substance is a nucleophilic compound.

Claim 10 (previously presented): The method of claim 9, wherein said nucleophilic compound is a thiol containing compound.

Claim 11 (withdrawn): A kit useful in determining if a substance is capable of regulating protein glycation, comprising a container means, and separate portions of each of (i) histone H1 and (ii) ADP-ribose.

Claim 12 (canceled)

**REMARKS**

Claims 1, 6 and 8 have been amended. Claims 4, 5 and 12 have been cancelled without prejudice and claim 11 was previously withdrawn from consideration. Thus, claims 1-3, 6, 8-10 are pending. Applicants now believe this application is in condition for allowance.

The Examiner rejected claims 1-6, and 8-10 under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification. Specifically, the Examiner argues there is no support in the specification for the phrase "wherein said substance is not aminoguanidine," because the disclosed screening method was open to the screening of all substances. As such, the Examiner maintains that the exclusion of aminoguanidine as a substance presents new matter.

The Examiner rejected claims 5 and 7 under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that substance (i) and aminoguanidine in claim 5 could be the same compound, thereby leading to confusion concerning the method. The Examiner also argued that the relationship between the two measurements in claims 5 and 7 was unclear. The Examiner indicated that careful reference to the scheme in Figures 2 and 10 and incorporation of such elements might advance the application to allowance.

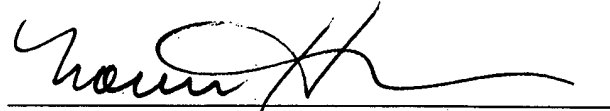
Based on these comments and a telephone interview between the Examiner and the undersigned on August 19, 2003, claim 1 has been amended to recite the screening method disclosed in Figures 2 and 10. The negative proviso "wherein said substance is not aminoguanidine" has been removed, thereby eliminating the new matter rejection under 35 U.S.C § 112, first paragraph. Applicants respectfully request withdrawal of this rejection.

Claim 1, as amended, also clarifies the relationships between the measurements and how these measurements are used to determine whether a substance inhibits glycation. Applicants believe that the rejection under 35 U.S.C § 112, second paragraph has been overcome and request withdrawal of this rejection.

All rejections have been addressed and overcome. Allowance of this application is believed proper and is urged.

Respectfully submitted,

FULBRIGHT & JAWORSKI, L.L.P.

A handwritten signature in black ink, appearing to read 'Norman D. Hanson', is written over a horizontal line.

Norman D. Hanson, Esq.  
Registration No. 30,946

666 Fifth Avenue  
New York, New York 10103-3198  
Telephone: 212-318-3168  
Telecopier: 212-318-3400